

IN THE CLAIMS

Please amend the claims as follows:

Claim 1 (Currently Amended): ~~Process for *in vitro* detection of resistance of cancer cells to oxaliplatin treatment, characterized in that it involves the measurement of the mitochondrial apoptosis of cancer cells that are treated or can or are to be treated with oxaliplatin~~

A process for detecting the resistance of a cancer cell to oxaliplatin treatment comprising:

detecting the expression of an effector or marker gene for mitochondrial apoptosis in a cancer cell;

wherein reduced expression of said effector or marker gene compared to a control cell not resistant to oxaliplatin indicates resistance to oxaliplatin.

Claim 2 (Currently Amended): The process of claim 1, wherein ~~Process according to claim 1, characterized in that the cancer is a cancer treated with oxaliplatin, in particular a~~ selected from the group consisting of colorectal cancer, a cancer of the ovaries, a cancer of the germinal cells, a cancer of the lung, a cancer of the digestive tract, a cancer of the prostate, a cancer of the pancreas, a cancer of the small intestine ~~[[or]]~~ and a cancer of the stomach.

Claim 3 (Currently Amended): The process ~~Process~~ according to claim 1 ~~or 2,~~ characterized in that it involves comprising the measurement of measuring the expression of at least one mitochondrial apoptosis gene.

Claim 4 (Currently Amended): The process of claim 1, comprising ~~Process~~ according to any of claims 1 to 3, ~~characterized in that it involves the measurement of~~

measuring the expression of at least one gene coding for a Bax, Bcl-2 or cytochrome c protein.

Claim 5 (Currently Amended): The process of claim 3, comprising ~~Process according to claim 3 or 4, characterized in that it involves the measurement of~~ detecting mRNA transcripts of the mitochondrial apoptosis gene(s).

Claim 6 (Withdrawn): The process of claim 1, comprising ~~Process according to claim 3 or 4, characterized in that it involves measurement of~~ detecting the amount and/or the activity of at least one mitochondrial apoptosis protein[[s]] in the cancer cells.

Claim 7 (Withdrawn): ~~Process~~ A process for *in vitro* detection of the resistance of cancer cells to oxaliplatin treatment ~~characterized in that it involves the detection of~~ comprising:

detecting at least one mutation indicative of deficient mitochondrial apoptosis in the case of treatment with oxaliplatin, in particular of a mutation in a region of the Bax gene containing a series of 8 deoxyguanines.

Claim 8 (Currently Amended): The process ~~Process~~ according to claim 1 ~~any of claims 1 to 6, characterized in that it involves~~ comprising:

a) ~~determination of~~ determining the level of mitochondrial apoptosis, and/or the level of expression of at least one mitochondrial apoptosis gene, in cancer cells ~~sampled~~ obtained from a patient;

b) ~~comparison to~~ comparing the level(s) measured with the level(s) measured in a corresponding control sample of cells not resistant to oxaliplatin.

Claim 9 (Withdrawn): ~~Process~~ The process according to claim 6 comprising:
~~, characterized in that it involves putting~~
~~contacting cancer cells together with an antibody capable of recognizing that~~
recognizes a mitochondrial apoptosis protein with a sample suspected of containing an
apoptosis protein, and
~~or a biologically active fragment, and the visualization of~~
detecting the formation of an antigen-antibody complex between said antibody and
said apoptosis protein;
~~the antigen-antibody complex possibly formed~~
wherein a reduced level of complex formation between said antibody and said
apoptosis protein compared to the level in a corresponding control cell not resistant to
oxaliplatin is indicative of resistance to oxaliplatin.

Claim 10 (Currently Amended): The process of claim 1, wherein a probe or primer is
used to detect the expression of at least one mitochondrial apoptosis gene ~~Process according~~
~~to any of claims 1 to 5, characterized in that it implements a primer or probe sequence~~
~~specific for the mitochondrial apoptosis gene.~~

Claim 11 (Currently Amended): The process of claim 10 comprising ~~Process~~
~~according to claim 10, characterized in that it involves:~~

a) ~~possible isolation of~~ isolating mitochondrial DNA from the a biological sample to
be examined, or the obtaining of a cDNA from the RNA of the biological sample or from
genomic DNA; and

b) ~~specific amplification of~~ amplifying the DNA from a) ~~by means of using~~ at least one primer for amplification of the an mitochondrial apoptosis gene.

Claim 12 (Currently Amended): ~~Process~~ The process according to claim 10, ~~characterized in that it involves~~ comprising:

a) contacting a nucleotide probe for ~~putting a nucleotide probe of an apoptosis gene together with the a biological sample to be analyzed for a time and under conditions suitable for hybridization to occur~~, the nucleic acid of the sample having, if need be, been previously made accessible to hybridization, under conditions allowing hybridization of the probe and the nucleic acid of the sample; and

b) detecting hybridization ~~visualization of the hybrid possibly formed.~~

Claim 13 (Withdrawn): ~~Process~~ A process for selection of compounds that inhibit the resistance of cancer cells to oxaliplatin comprising; ~~characterized in that it involves~~:

a) ~~addition of~~ adding at least one candidate compound to the cancer cells resistant to oxaliplatin;

b) ~~comparison of~~ comparing the level of mitochondrial apoptosis and/or expression of at least one apoptosis gene in the presence and absence of the compound;

c) ~~deduction of~~ deducing the anti-resistance effect when the level of mitochondrial apoptosis is greater after addition of the compound, or when the level of expression is greater when the gene is a gene that stimulates mitochondrial apoptosis, or when the level of expression is less when the gene is a gene that inhibits mitochondrial apoptosis.

Claims 14-16 (Cancelled)

Claim 17 (Withdrawn): ~~Product~~ A composition containing:

oxaliplatin and

~~an agent stimulating mitochondrial apoptosis, in particular chosen from among~~
selected from the group consisting of TNF, FasL, glutamate, Herbimycin A, Paraquat,
inhibitors of protein kinase such as Staurosporine, Calphostin C, derivatives of d-erythro-
sphingosine, Chelerythrine chloride, inducers of MAP kinase such as Anisomycin and
inducers of MPT;

wherein said product is formulated as a combination product for simultaneous use,
~~separated or spaced apart in time as an anti-cancer agent.~~

Claim 18 (Withdrawn): ~~Composition~~ A composition consisting of

oxaliplatin and

at least one anti-resistance agent capable of stimulating mitochondrial apoptosis;
~~chosen from among~~ selected from the group consisting of TNF, FasL, glutamate, Herbimycin
A, Paraquat, inhibitors of protein kinase such as Staurosporine, Calphostin C, derivatives of
d-erythro-sphingosine, Chelerythrine chloride, inducers of MAP kinase such as Anisomycin
and inducers of MPT; and

optionally at least one pharmaceutically acceptable excipient or carrier.

Claim 19 (Withdrawn): ~~Kit~~ A kit for diagnosis of resistance of a cancer to oxaliplatin
~~characterized in that it includes~~ comprising:

- a) at least one compartment suitable to contain a probe;
- b) ~~possibly the~~ reagents necessary for the implementation of a hybridization reaction;
- c) ~~possibly~~ at least one primer and the reagents necessary for a DNA amplification
reaction.

Claim 20 (Withdrawn): Cell HCT116/S as registered on 16 June 2003, under number: I-3051, with the Collection Nationale de Cultures de Microorganismes (CNCM), Pasteur Institute, Paris, France.

Claim 21 (Withdrawn): ~~Use of~~ A method for using cell HCT116/S according to claim 20, or of any cell derived from this cell HCT116/S, to study the correlation between the resistance of cancer cells, most preferably colorectal, to anti-cancer treatment and the expression of a mitochondrial apoptosis gene.

Claim 22 (Withdrawn): ~~Use of~~ A method of using cell HCT116/S according to claim 20, or of any cell derived from this cell HCT116/S, for the visualization and identification of a mitochondrial apoptosis gene whose expression is linked to the resistance of cancer cells, most preferably colorectal, to anti-cancer treatment.

Claim 23 (Withdrawn): ~~Use of~~ A method for using cell HCT116/S according to claim 20, or of any cell derived from this cell HCT116/S, for the selection of a compound capable of stimulating mitochondrial apoptosis in a cancer cell, said compound being designed to be combined with an anti-cancer agent to which said cancer cell is resistant, most preferably said anti-cancer agent to which said cancer cell is resistant being oxaliplatin and, as the case may be, said cell is a colorectal cancer cell.

Claim 24 (New): The process of claim 1, wherein said effector or marker gene expresses a pro-apoptotic Bax protein, said cancer cell is a colorectal cancer cell, and said detecting comprises detecting the level of expression of mRNA encoding

Bax, wherein reduced expression of mRNA encoding Bax compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin.

Claim 25 (New): The process of claim 1, wherein said effector or marker gene expresses a pro-apoptotic Bak protein, said cancer cell is a colorectal cancer cell, and said detecting comprises detecting the level of expression of mRNA encoding Bak, wherein reduced expression of mRNA encoding Bak compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin.